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Antihistamine was applied to the cut dentin surface of thermally traumatized monkey teeth and the cavity preparation restored with zinc-oxide eugenol. Control teeth were similarly traumatized and restored without antihistamine treatment. Histologic examination of the pulps did not demonstrate any significant effect of antihistamine on pulpal inflammation during a 4-96 hour period.

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THE EFFECT OF TOPICAL ANTIHISTAMINE ON THE INITIAL PULPAL INFLAMMATORY RESPONSE OF MONKEY TEETH

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ABSTRACT

Cavity preparations were made in sixty sound teeth of healthy monkeys. Thermal trauma was delivered to the pulps of all teeth through application of a heated soldering iron to the floor of a cavity preparation. Fifteen teeth were randomly designated as controls and were restored immediately with zinc oxide-eugenol.

Forty-five teeth were designated as test teeth and treated topically with a four percent antihistamine solution, and restored with zinc oxide-eugenol.

Histologic sections were prepared to show the effect of the antihistamine on the thermally initiated inflammatory response during the post operative period.

No significant difference was observed in the inflammatory reaction of treated or untreated pulps. A four percent aqueous solution of topically applied antihistamine did not appear to be of any significant value in obviating pulpal inflammation.

THE EFFECT OF TOPICAL ANTIHISTAMINE ON THE INITIAL PULPAL INFLAMMATORY RESPONSE OF MONKEY TEETH

INTRODUCTION

Following pulpal trauma, the damaged tissue cells liberate substances capable of initiating an inflammatory response. Histamine is one of the more potent mediators and exerts histochemical and neuronal effects resulting in vascular dilatation, capillary permeability and stimulation of pain receptors.[1]

A recently published investigation has shown the histamine levels in pulpal tissue increase markedly following thermal insult.[2] Consideration of the high level of histamine in injured pulp and its potential for severe inflammatory effects, raises the question of the therapeutic value of antihistamine in pulp dressings.

The physiologic antagonists of histamine are the antihistamines which are a group of phenolic esters that inhibit the effects of histamine, particularly the increased capillary permeability and extra cellular edema.[3]

Pyribenzamine* is a heterocyclic amine with marked antihistaminic properties that has been shown effective in reducing histamine related edema.[4]

The purpose of the present study is to evaluate histologically the effect of topical application of Pyribenzamine on the initial inflammatory reaction following thermal injury of monkey pulpal tissue.

MATERIAL AND METHODS

Sixty teeth from three 5-7 kg male Macaca fascicularis monkeys were traumatized by contacting the pulpal floor of a class five cavity preparation with the tip of an electric soldering iron heated to 71°C. Tip temperature was controlled by a variable rheostat, and tip size and contour were altered to provide maximum contact with the cavity floor. The injurious thermal effects of

* Pyribenzamine (tripelennamine) Ciba Pharmacertical Company, Summit, N.J.

the procedure were expected to induce a measurable inflammatory response similar to that reported in dog pulps by Lisanti and Zander.[5]

Each animal had five control teeth randomly selected to demonstrate the initial pulpal effects of the thermal stimulation alone, and fifteen teeth selected to study the effect of 4 percent topical solution of pyribenzamine on the response to thermal injury.

Following anesthetization of the animals with 20 percent Sernylan (0.7cc to 1.0cc I.M.) and Pentobarbital* (0.2cc to 0.5cc I.V.), cavity preparations were made on the isolated teeth using new number 35 carbide burs, rotated at high speed with air and coolant spray. Cavity preparations were class 5 with dimensions of 2 by 4 millimeters in the labial surface, and to the depth of the bur head.

The preparations were flushed with 10 cc sterile distilled water and dried with sterile cotton. The heated soldering iron was applied for 10 seconds at a tip temperature of 71°C. Control teeth were then immediately restored with zinc oxide and eugenol. Teeth treated with the antihistamine had 1 drop (.05 ml) of 4 percent aqueous pyribenzamine applied with a micropipette to the washed and dried dentin surface. After one minute, the cavity was flushed with 10 cc sterile distilled water, dried with sterile cotton and restored with zinc oxide-eugenol.

At each post operative interval of 4, 24, and 96 hours, an animal was anesthetized and sacrificed by whole body perfusion with 10 percent formalin. The teeth were dissected from the alveolus, the apical third of the root clipped, and the teeth were placed in 10 percent formalin for further fixing. The teeth were decalcified and prepared for histologic examination following the techniques of Stanley and Weaver.[6]

*Sernylan (Phencyclidine Hydrochloride), Bio-ceutic Labs, St. Joseph, Mo.
*Sodium Pentobarbital Injection, Pitman-Moore, Washington Crossing, N.J.

The degree of pulpal response of all teeth was graded histologically through microscopic examination of serial sections. Only sections having recognizable dentinal tubules extending from cavity floor to pulp chamber and remaining dentin thicknesses of 0.5 to 1.8 mm were scored. Each tooth was given a pulpal inflammatory score obtained through averaging the scores given for three parameters of initial pulpal inflammatory response; (1) odontoblastic degeneration; (2) Capillary effects (dilation and focal hemorrhage); (3) Cellular displacement into the pulpal end of dentinal tubules.[7] Results were then segregated into post operative sacrifice intervals of 4, 24, and 96 hours and grouped according to control or experimental status.

RESULTS

All specimens, control and experimental, in 4, 24, and 96 hours sacrifice groups, showed evidence of acute inflammatory response to the thermal stimulus, however, the degree of response observed between control and experimental samples was similar.

Inflammation in the 4 hour post operative group was evidenced by edematous changes in the odontoblastic layer with odontoblast spacing and separation from the predentin layer. The capillary effect, evidenced by dilation of the microvessels and occasional collections of extravasated erythrocytes, was minimal at this stage. The relative numbers of dentinal tubules showing intratubular odontoblasts, recorded as the tubule effect, were not marked in this early stage of inflammatory reaction.

The 24 hour specimens all showed marked disorganization of the normal pallisaded arrangement of the odontoblasts with vacuolization or microblisters seen between the cells. Cell detail in the odontoblastic layer was indistinct, and odontoblast numbers reduced in comparison to the 4 hour group. Many odontoblasts were displaced into the dentinal tubules and in comparison with the 4 hour specimens, the capillary effects and focal hemorrhages were marked.

The 96 hour specimens were similar to the 24 hour group with marked edema in the cell free layer and throughout the pulp. The capillary response was exaggerated, with a network of swollen capillaries appearing near the odontoblastic layer in association with areas of hemorrhage and hemosiderin pigmentation.

Most of the sections showed the area contacted by the soldering iron as a dark semilunar zone of tubular disturbance and the inflammatory responses seen were confined to an area of pulp in direct approximation with the tubules. In no instance was any appreciable inflammatory cell infiltrate observed.

Average inflammation scores for control pulps (burn with no antihistamine) were compared to inflammatory scores of test pulps (burn plus antihistamine), for each of the intervals of 4, 24 and 96 hours. Results were analyzed for significance using the Chi square analysis with a degree of freedom of 1.0 and a critical value of 3.84 at the 0.05 level of significance.

Analysis of data obtained from the 4 hour group of control and test pulps revealed a Chi square value of 0.94 which was not significant. Similar analysis of the 24 and 96 hour groups (Chi square values of 0.65 and 0.22 respectively) did not show a significant difference in inflammatory response between control and antihistamine treated pulps.

DISCUSSION

Based on the finding that histamine levels increase sharply following pulpal trauma, the suggestion has been made that antihistamines might prove therapeutically valuable as pulp dressings.[2] No previous studies of antihistamine effects on the dental pulp have been published and this investigation was designed to provide information on a potential therapeutic modality.

The results of the Chi square tests of the 4, 24, and 96 hour samples demonstrate that an antihistamine topically applied to an injured pulp does not mitigate the initial inflammatory response.

Among the many factors which can adversely influence the results of this research are; dosage, duration of application, route of administration, type of antihistamine, and restorative material used. However, the most probable explanation of the ineffectiveness of antihistamine used in this manner, is that it acts as a competitive inhibitor. Antihistamine must be "on site" at the tissue level prior to the liberation of histamine in order to forestall the histamine effects. Antihistamine cannot resolve any of the histamine induced inflammatory response once initiated nor can it prevent the further liberation of histamine later on in the post traumatic period.

This investigation would tend to substantiate a pharmacological prediction that antihistamine would fail to affect an injured pulp unless the pulp tissues were preloaded with the drug. The question still exists whether antihistamines could favorably influence the pulpal response to trauma, if prophylactically administered enterally or parenterally.

It is felt therefore, considering the pharmacologic actions of antihistamines and the results of this investigation, that no appreciable degree of anti-inflammatory effect should be anticipated through the incorporation of antihistamine in pulp dressings.

SUMMARY

A four percent aqueous solution of antihistamine applied to a cavity preparation did not influence the pulpal inflammation induced by thermal trauma. It is not believed that antihistamine would prove therapeutically valuable as a pulp medication.

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In conducting the research described in this manuscript, the investigators adhered to the "Guide for the Care and Use of Laboratory Animals," as promulgated by the Committee on the Guide for Laboratory Animal Facilities and Care of the Institute of Laboratory Animal Resources, National Academy of Sciences-National Research Council.